EVALUATION CRITERIA FOR COVID-19 SEROLOGY SCREENING

INTENDED AUDIENCE: CALIFORNIA STATE TESTING TASK FORCE MEMBERS, CLINICAL LABORATORY DIRECTORS, AND INFECTIOUS DISEASE PHYSICIANS

GOAL: Provide step-by-step guidance on how to evaluate anti-SARS-CoV-2 serology assays and testing platforms.

BACKGROUND
The novel coronavirus disease (COVID-19) pandemic has prompted the urgent need for high performing molecular (PCR) and serology tests for COVID-19. With molecular pathogen detection more readily available, there has been a shift towards serological screening to determine prior exposure to SARS-CoV-2 infection. These serology assays measure antibodies against SARS-CoV-2.

FREQUENTLY ASKED QUESTIONS

- *Where can serological tests be performed?* At this time, most platforms are considered high complexity under the Clinical Laboratory Improvement Amendment (CLIA) and must be performed at high complexity labs. Point-of-care kits that receive FDA emergency use authorization are an exception and are considered CLIA-waived for the duration of the national emergency declaration.

- *What types of serological testing formats exist?* Testing formats range from simple disposable lateral flow assays (LFA) used as a point-of-care test to enzyme linked immunosorbent assays (ELISA) or automated chemiluminescent immunoassays run on large instruments in clinical laboratories.

- *Are rapid disposable serology test kits (lateral flow assays) reliable?* No, rapid disposable serology test kits are of uncertain reliability. Since the FDA did not require Emergency Use Authorization, many of these disposable tests have not been fully validated and the performance characteristics are not well established. They are not recommended for individual use.

- *What considerations are there for using serology tests to predict COVID-19 prevalence?* The screening performance of these tests in predicting disease (positive and negative predictive value) will vary depending on the prevalence of COVID-19 in the population tested. For example, at the nursing home in Washington state where 30.3% of the people tested positive for COVID-19 by PCR, the PPV of a serology test with 90% sensitivity and 97% specificity will be high (93%). In contrast, if there is a 3% prevalence rate as seen in some occupational health settings, the PPV of a serology test with 90% sensitivity and 97% specificity will be low (47%).

- *What considerations are there for using serology tests to predict antibody production?* The prevalence of disease also influences the PPV for predicting antibody production following COVID-19 exposure.

ASSESSMENT SCHEME

Step 1.
> Do you have the equipment needed to serology testing? If not, is it available or back-ordered? If back-ordered, consider investigating a different platform

Step 2.
> Was the test validated using samples from known COVID-19 positive patients?
> If NO, DO NOT USE

Step 3.

> Does the test meet your needs for:
> - Turnaround time
> - Test throughput
> - Level of automation
> - Space for equipment
> - Reagent availability
>
> If NO, DO NOT USE

Step 4.

> What is the estimated prevalence of COVID-19 in the population targeted for serology testing?

Step 5.

> Based on estimated prevalence, does the test have adequate clinical sensitivity and specificity for the targeted population? (See Table 1)

Table 1: Positive Predictive Value Comparison based on Test Characteristics

	Sensitivity 90% Specificity 97%	Sensitivity 90% Specificity 98%
Prevalence	PPV	PPV
1%	23%	31%
3.5%	52%	62%
5%	61%	70%
6%	66%	74%
7%	69%	77%
8%	72%	79%
9%	75%	82%
10%	77%	83%

Test acceptability criteria of Sensitivity and Specificity of 90% and 97% will provide 77% PPV at a COVID-19 prevalence of 10%.

Sensitivity: Ability of the test to correctly identify those patients with the disease.
Specificity: Ability of the test to correctly identify those patients without the disease.
Prevalence: The proportion of a population that have the disease.
Positive Predictive Value: How likely is it that a patient has the disease given that the test result is positive.